

SECOND PRELIMINARY AMENDMENT
METHOD AND APPARATUS FOR QUANTIFYING TISSUE HISTOLOGY
Attorney Docket No. 142.019US01

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Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of claims:

1. (Original) A method of analysing at least one parameter of a body component, comprising the steps of illuminating the component or body with light of at least a first and second waveband, receiving light of at least said first and second wavebands remitted by the component at a photoreceptor or photoreceptors, and analysing the light received at the photoreceptor (s) to provide a ratio between the amount of light remitted of the first waveband and the amount of light remitted of the second waveband, and from this calculating the component parameter.
2. (Original) A method according to claim 1, in which the wavebands are predetermined and calculated by use of a mathematical model of the body component and its characterising parameters.
3. (Original) A method according to claim 1, in which the wavebands are predetermined and derived through use of a biological model of the body component.
4. (Original) A method of analysing at least one parameter of a body component, comprising the steps of illuminating the body or component with light of at least a first and second waveband, receiving light of at least said first and second wavebands remitted by the component at the photoreceptor (s), but eliminating light reflected by the component or body and analysing the light received at the photoreceptor (s) to provide a ratio between the amount of light of the first waveband and the amount of light of the second waveband, and from this calculating the component parameter.
5. (Previously Presented) A method according to claim 4 where the wavebands are chosen such that the component parameter is a one to one function of the ratio between the amount of light remitted by the body component of the first waveband and the amount of light

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remitted by the component of the second waveband.

6. (Previously Presented) A method according to claim 4, in which the waveband ratios are compared with a mathematically generated model of waveband ratios corresponding to a range of component parameters.
7. (Previously Presented) A method according to claim 4, in which the waveband ratios are compared with an experimentally measured set of waveband ratios corresponding to a range of component parameters.
8. (Previously Presented) A method according to claims 6 where the comparison results in a measure or measures relating to the component parameter or parameters.
9. (Previously Presented) A method according to claim 4 where a function is derived relating the computed ratios and the component parameter or parameters.
10. (Previously Presented) A method according to claim 4, in which the light reflected by the component is eliminated by the use of a pair of cross polarised linear polarizing filters, one filter being placed between the source of illumination and the component, and the other filter placed between the component and the photoreceptor or photoreceptors.
11. (Previously Presented) A method according to claim 4 in which the light illuminating the body component is a light of a plurality of wavelengths which includes at least the wavebands.
12. (Original) A method according to claim 11 in which the illuminating light is ambient light.
13. (Original) A method according to claim 11 in which the illuminating light is sunlight.
14. (Previously Presented) A method according to claims 11, in which at least one filter

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is placed sequentially between the source of illumination and the component or between the component and the photoreceptor or photoreceptors.

15. (Previously Presented) A method according to claim 4, in which the body component is human or animal tissue.

16. (Original) A method according to claim 15, in which the tissue is one of skin, the lining of the gut, colon, oesophagus, cervix, eye or any other epithelial tissue.

17. (Previously Presented) A method according to claim 4, for analysing a plurality of body component parameters where the component is illuminated with light of each of a collection of wavebands. The light received by the photoreceptor or photoreceptors includes this collection of wavebands. The light is analysed at the photoreceptor (s) to provide a collection of ratios between the amount of light of each waveband with some or all of the other wavebands and from this calculating the component parameter (s).

18. (Previously Presented) A method according to claim 4, for analysing a plurality of body component parameters in which for each component parameter there exists a pair of predetermined wavebands such that the component parameter is a one to one function of the ratio between the amount of light remitted by the component of the first predetermined waveband of the pair and the amount of light remitted by the component of the second predetermined waveband of the pair, and the component is illuminated with light of each pair of predetermined wavebands, the light received by the photoreceptor or photoreceptors is of each pair of predetermined wavebands remitted by the component at the photoreceptor (s), and analysing the light received at the photoreceptor (s) to provide for each component parameter a ratio between the amount of light of the first waveband and the amount of light of the second waveband, and from this calculating each component parameter.

19. (Previously Presented) A method according to claim 17, in which the waveband ratios are compared with a mathematically generated model of waveband ratios corresponding to a range of component parameters to ascertain the component values.

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20. (Previously Presented) A method according to claim 17, in which the waveband ratios are compared with an experimentally measured set of waveband ratios corresponding to a range of component parameters to ascertain the component values.
21. (Previously Presented) A method according to claims 19 where the comparison results in a measure or measures relating to the component parameter or parameters.
22. (Previously Presented) A method according to claims 19 where a function is derived relating the computed ratios and the component parameter or parameters.
23. (Previously Presented) A method according to claim 4 in which the body component is skin and the parameters are the concentration of melanin and the concentration of blood.
24. (Original) A method according to claim 23, in which the predetermined wavebands are the Red, Green and Blue colour bands, with the three wavebands providing the two ratios which are a one to one function with the parameters.
25. (Previously Presented) A method according to claim 4, in which the predetermined wavebands have been calculated by the steps of:
- 1) defining a set of potential wavebands
 - 2) defining one or more image ratios, the or each image ratio for a region being obtained by dividing the amount of light remitted by the component of a given waveband for that region, the "image value" for that filter, by another image value for that same region;
 - 3) for a component parameter to be analysed and for said defined set of potential wavebands and for said given image ratios, obtaining a function mapping points in parameter space to points in image ratio space;
 - 4) determining whether the mapping function provides a 1: 1 correspondence between points in parameter space and points in image ratio space; and
 - 5) if the mapping function does not provide a 1: 1 correspondence, rejecting said potential wavebands, repeating steps 1) to 4) and, if the mapping function does provide a 1: 1

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correspondence accepting the potential wavebands as a candidate set of predetermined wavebands.

26. (Original) Apparatus for analyzing at least one parameter of component, comprising a light source for illuminating the component with light of at least a first and second predetermined waveband, a photoreceptor or photoreceptors for receiving light of at least said first and second predetermined wavebands remitted by the component reflected by the surface at a photoreceptor or photoreceptors; surface reflection elimination means for eliminating light reflected by the surface of the component and means for analyzing the light received at the photoreceptor (s) to provide a ratio between the light of the first waveband and the light of the second waveband, and from this calculating the component parameter.

27. (Previously Presented) Apparatus according to claim 26 where the predetermined wavebands are chosen such that the component parameter is a one to one function of the ratio between the amount of light remitted by the component of the first predetermined waveband and the amount of light remitted by the component of the second predetermined waveband.

28. (Original) Apparatus according to claim 26, in which the photoreceptor comprises a digital camera.

29. (Original) Apparatus according to claim 28, in which the digital camera includes a plurality of filters, one for each predetermined waveband.

30. (Original) Apparatus according to claim 26 in which the light source is ambient light.

31. (Previously Presented) Apparatus according to claim 27, in which the distance between the photoreceptor (s) and the component is between 0.5cm and 10m.

32. (Previously Presented) Apparatus according to ~~any one of~~ claims 33, in which the distance between the light source and the component is between 0. 5cm and 10m.

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33. (Original) A method for deriving a pair of predetermined wavebands suitable for use in analysing a given parameter of a body component, the method comprising the steps of:

- 1) defining a set of potential wavebands
- 2) defining one or more image ratios, the or each image ratio for a region being obtained by dividing the amount of light remitted by the component of a given waveband for that region, the "image value" for that filter, by another image value for that same region;
- 3) for the parameter of the component to be analysed and for said defined set of potential wavebands and for said given image ratios, obtaining a function mapping points in parameter space to points in image ratio space;
- 4) determining whether the mapping function provides a 1: 1 correspondence between points in parameter space and points in image ratio space; and
- 5) if the mapping function does not provide a 1 : 1 correspondence, rejecting said potential wavebands, repeating steps 1) to 4) and, if the mapping function does provide a 1: 1 correspondence accepting the potential wavebands as a candidate set of predetermined wavebands.

34. (Original) A method according to claim 33 and comprising, for a set of potential wavebands accepted as a candidate set of wavebands, determining the accuracy of parameter recovery obtained using said mapping function and determining whether or not the accuracy is sufficient or matches some other criterion.

35. (Original) A method according to claim 34, wherein if the accuracy is sufficient or matches said criterion, the candidate wavebands are adopted and if the accuracy is not sufficient or does not match said criterion, steps 1) to 5) are repeated for a different set of wavebands.

36. (Previously Presented) A method according to claim 34, wherein the accuracy is determined by:

- a) calculating the error associated with image acquisition for each vector of each image ratio;
- b) from the image ratio vector error, calculating the maximum possible error in each

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component of the parameter vector across the whole of parameter space; and

c) using the vector of parameter errors at each point within parameter space to measure the accuracy of parameter recovery.

37. (Previously Presented) A method according to claim 33 and comprising repeating steps 1) to 5) for a multiplicity of sets of potential wavebands to identify a plurality of candidate waveband sets, determining for each candidate set an error value representing the accuracy of parameter recovery obtained using the corresponding mapping function, and using said candidate set as a basis for determining a preferred set of wavebands.

38. (Original) A method according to claim 37 and comprising using a genetic algorithm to determine a preferred set of wavebands using said candidate set.

39. (Previously Presented) A method according to claim 33 and comprising using a gradient descent algorithm to select an optimal set of wavebands, the starting point for the algorithm being a first candidate set of wavebands identified in step 4).

40. (Previously Presented) A method according to claim 33, wherein for each waveband the method of the present invention is used to determine the center wavelength of the waveband.

41. (Previously Presented) A method according to claim 33, wherein the method is used to determine the full width half maximum (FWHM) of the waveband.

42. (Previously Presented) A method according to claim 33, wherein step 3) comprises constructing a Jacobian matrix for the mapping function with respect to said parameter (s), and obtaining the determinant of that matrix.

43. (Original) A method of determining a property or properties of each of a set of filters, which filters are used to select specific wavelength ranges in a system which relies upon a spectral analysis of remitted, emitted, and/or transmitted light to quantify a parameter or

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parameters of an object or material, the method comprising the steps of:

- 1) defining a set of potential filter properties;
- 2) defining one or more image quotients, the or each image quotient for a region being obtained by dividing the quantified output of a given filter for that region, the "image value" for that filter, by another image value for that same region;
- 3) for an object or material to be analysed and for said defined set of potential filter properties and for said given image quotients, obtaining a function mapping points in parameter space to points in image quotient space;
- 4) determining whether the mapping function provides a 1 : 1 correspondence between points in parameter space and points in image quotient space; and
- 5) if the mapping function does not provide a 1 : 1 correspondence, rejecting said potential filter properties, repeating steps 1) to 4) and, if the mapping function does provide a 1 : 1 correspondence accepting the potential filter properties as a candidate set of filter properties.

44. (Original) Apparatus for analysing an object or material having means for conducting a spectral analysis of remitted, emitted, and/or transmitted light to quantify a parameter or parameters of an object or material, the apparatus comprising a plurality of filters for splitting said light into respective components, the filters having properties obtained by using the method of the claim 43.

45. (New) Apparatus for determining the distribution of chromophores and/or the thickness of structural layers in a sample of epithelial tissue, the apparatus comprising:

a polarized light source operable to illuminate a sample of epithelial tissue with polarized light having wavelengths falling within a first, second, and third predetermined wavebands;

a polarizing filter positioned so as to filter light remitted from a sample of epithelial tissue said polarizing filter being such to filter out light polarized in the manner generated by said polarized light source;

an image generator operable to detect filtered remitted light from a sample of epithelial tissue and generate image data indicative of the intensity of filtered remitted light received by said image generator having wavelengths falling within said first, second and third predetermined

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wavebands;

a ratio determination module operable to process image data generated by said image generator to determine for positions within images represented by said image data, a first ratio corresponding to the ratio of light received by said image generator having wavelengths within said second waveband relative to light having wavelengths within said first waveband, and a second ratio corresponding to the ratio of light received by said image generator having wavelengths within said third waveband relative to light having wavelengths within said first waveband;

a concentration determination module operable to determine for positions within an image represented by image data generated by said image generator the concentrations of chromophores and/or the thickness of structural layers of said epithelial tissue at said positions in a sample of epithelial tissue represented by said image data utilizing said first and said second ratios determined for said positions by said ratio determination module; and

an output module operable to output data representing determined concentrations of chromophores and/or thickness of structural layers for points a sample of epithelial tissue as determined by said concentration determination module.

46. (New) Apparatus in accordance with claim 45 wherein said image generator comprises a digital camera.

47. (New) Apparatus in accordance with claim 45 wherein said first waveband comprises a waveband corresponding to red light.

48. (New) Apparatus in accordance with claim 45 wherein said second waveband comprises a waveband corresponding to green light.

49. (New) Apparatus in accordance with claim 45 wherein said third waveband comprises a waveband corresponding to blue light.

50. (New) Apparatus in accordance with claim 45 wherein said first waveband comprises a waveband centered on a wavelength of 700nm

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51. (New) Apparatus in accordance with claim 45 wherein said second waveband comprises a waveband centered on a wavelength of 560nm.

52. (New) Apparatus in accordance with claim 45 wherein said third waveband comprises a waveband centered on a wavelength of 473nm.

53. (New) Apparatus in accordance with claim 45 wherein one of said first, second or third wavebands comprises infra red light.

54. (New) Apparatus in accordance with claim 45 wherein said concentration determination module comprises a look up table associating pairs of first and second ratios generated by said ratio determination module with items of data identifying concentrations of blood and melanin which when illuminated with polarized light are liable to remit cross polarized light having wavelengths falling within said first, second and third wavebands at said first and second ratios.

55. (New) Apparatus in accordance with claim 54 wherein said pairs of first and second ratios and said concentrations of blood and melanin comprise ratios and concentrations determined by analyzing samples of epithelial tissue.

56. (New) Apparatus in accordance with claim 54 wherein said pairs of first and second ratios and said concentrations of blood and melanin comprise ratios and concentrations determined utilizing a mathematical model of the expected remittance of illuminated light by samples of epithelial tissue having differing concentrations of blood and melanin.

57. (New) Apparatus in accordance with claim 45 wherein said concentration determination module is operable to determine values representative of concentrations of blood and melanin by applying a predetermined mathematical function to first and second ratios for a position as determined by said ratio determination module.

58. (New) Apparatus in accordance with claim 45 wherein said concentration determination

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module comprises a look up table associating pairs of first and second ratios generated by said ratio determination module with items of data identifying concentrations of blood and tissue thickness which when illuminated with polarized light are liable to remit cross polarized light having wavelengths falling within said first, second and third wavebands at said first and second ratios.

59. (New) Apparatus in accordance with claim 58 wherein said pairs of first and second ratios and said concentrations of blood and tissue thickness comprise ratios and concentrations determined by analyzing samples of epithelial tissue.

60. (New) Apparatus in accordance with claim 58 wherein said pairs of first and second ratios and said concentrations of blood and melanin comprise ratios and concentrations determined utilizing a mathematical model of the expected remittance of illuminated light by samples of epithelial tissue having differing concentrations of blood and tissue thickness.

61. (New) Apparatus in accordance with claim 45 wherein said concentration determination module is operable to determine values representative of concentrations of blood and tissue thickness by applying a predetermined mathematical function to first and second ratios for a position as determined by said ratio determination module.

62. (New) Apparatus in accordance with claim 45 wherein said polarized light source operable to illuminate a sample of epithelial tissue with polarized light comprises:

a light source; and

a polarizing filter arranged to polarize light generated by said light source.

63. (New) Apparatus in accordance with claim 62 wherein said light source is operable to illuminate a sample of epithelial tissue sequentially with light having wavelengths falling within different ones of said first, second, and third predetermined wavebands.

64. (New) A method for determining the distribution of chromophores and/or thickness of structural layers in a sample of epithelial tissue, the method comprising:

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illuminating a sample of epithelial tissue with polarized light having wavelengths falling within a first, second, and third predetermined wavebands;

filtering light remitted from a sample of epithelial tissue so as to filter out light polarized in the manner corresponding to the polarized light utilized to illuminate the sample of epithelial tissue;

generating image data indicative of the intensity of filtered remitted light having wavelengths falling within said first, second and third predetermined wavebands;

processing generated image data to determine for positions within images represented by said image data, a first ratio corresponding to the ratio of filtered remitted light having wavelengths within said second waveband relative to filtered remitted light having wavelengths within said first waveband, and a second ratio corresponding to the ratio of filtered remitted light having wavelengths within said third waveband relative to filtered remitted light having wavelengths within said first waveband;

determining for positions within an image represented by generated image data the concentrations of chromophores and/or thickness of structural layers of said epithelial tissue at said positions in the sample of epithelial tissue represented by said image data utilizing said first and said second ratios determined for said positions; and

outputting data representing said determined concentrations of chromophores and/or thickness of epithelial tissue for points in said sample of epithelial tissue.

65. (New) A method in accordance with claim 64 wherein said first waveband comprises a waveband corresponding to red light.

66. (New) A method in accordance with claim 64 wherein said second waveband comprises a waveband corresponding to green light.

67. (New) A method in accordance with claim 64 wherein said third waveband comprises a waveband corresponding to blue light.

68. (New) A method in accordance with claim 64 wherein one of said first, second or third wavebands comprises infra red light.

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69. (New) A method in accordance with claim 64 wherein said first waveband comprises a waveband centered on a wavelength of 700nm.

70. (New) A method in accordance with claim 64 wherein said second waveband comprises a waveband centered on a wavelength of 560nm.

71. (New) A method in accordance with claim 64 wherein said third waveband comprises a waveband centered on a wavelength of 473nm.

72. (New) A method in accordance with claim 64 wherein said determining for positions within an image represented by generated image data the concentrations of chromophores and/or thickness of structural layers of said epithelial tissue comprises determining for positions within an image represented by generated image data the concentrations of blood and melanin in said epithelial tissue at said positions in the sample of epithelial tissue represented by said image data utilizing said first and said second ratios determined for said positions.

73. (New) A method in accordance with claim 64 wherein said determining for positions within an image represented by generated image data the concentrations of chromophores and/or thickness of structural layers of said epithelial tissue comprises determining for positions within an image represented by generated image data the concentrations of blood in said epithelial and tissue thickness of said epithelial tissue at said positions in the sample of epithelial tissue represented by said image data utilizing said first and said second ratios determined for said positions.

74. (New) A method in accordance with claim 64 wherein said illuminating a sample of epithelial tissue with polarized light having wavelengths falling within a first, second, and third predetermined wavebands comprises sequentially illuminating said sample of epithelial tissue with polarized light having wavelengths falling within different ones of said first, second and third predetermined wavebands.